Early Reactions to Harvey's Circulation Theory:

The Impact on Medicine

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Abstract

In early 17th century Europe, scientific concepts were still based largely on ancient philosophical and theological explanations. During this same era, however, experimentation began to take hold as a legitimate component of scientific investigation. In 1628, the English physician William Harvey announced a revolutionary theory stating that blood circulates repeatedly throughout the body. He relied on experimentation, comparative anatomy and calculation to arrive at his conclusions. His theory contrasted sharply with the accepted beliefs of the time, which were based on the 1400-year-old teachings of Galen and denied the presence of circulation. As with many new ideas, Harvey's circulation theory was received with a great deal of controversy among his colleagues. An examination of their motives reveals that many proponents agreed with his theory largely because of the logic of his argument and his use of experimentation and quantitative methods. However, some proponents agreed for religious, mystical and philosophical reasons, while some were convinced only because of the change in public opinion with time. Many opposed the circulation theory because of their rigid commitment to ancient doctrines, the questionable utility of experimentation, the lack of proof that capillaries exist, and a failure to recognize the clinical applications of his theory. Other opponents were motivated by personal resentments and professional "territorialism." Beyond the immediate issues and arguments, however, the controversy is important because it helped establish use of the scientific method.

Key Words: William Harvey, circulation, medical history, scientific method.

IN 1628, THE ENGLISH PHYSICIAN William Harvey (1578–1657) published his *Exercitatio anatomica de motu cordis et sanguinis in animalibus (Anatomical studies on the motion of the heart and blood)*. Using experimentation, comparative anatomy and calculation, he startled the scientific world by demonstrating that the heart circulates blood repeatedly throughout the body (Fig. 1) (1).

As with many new theories, Harvey's was controversial because it clashed with the leading dogmas of the time. Brimming with inconsistencies (1, 2), the governing doctrine concerning the heart and blood was based on the teachings of the ancient Greek physiologist Galen and had sufficed for more than 1400 years. Galen taught that food traveled to the liver, where it was transformed into blood (Fig. 2). Veins emanating from the liver carried blood throughout the body; some of these veins crossed through septal pores from the right to the left ventricle. Galen claimed that venous blood nourished the lungs—but no pulmonary circuit was recognized. Inhaled life-sustaining "spirits" supposedly mixed with blood in the left ventricle, where together they were expelled into the arteries by the innate heat of the heart. With the single exception of pores in the interventricular septum, there was no mention of a communication between arteries and veins (2, 3). (Capillaries were discovered in 1660 by Marcello Malpighi [3]).

Although some people knew of the pulmonary circulation and one-way valves (2, 3), it is fair to conclude that the function of the heart, blood, and vasculature was largely misunderstood prior to Harvey. Given this environment of confusion, it is not surprising that Harvey's claims received so much criticism. Surely Harvey had anticipated this, since in chapter 8 of

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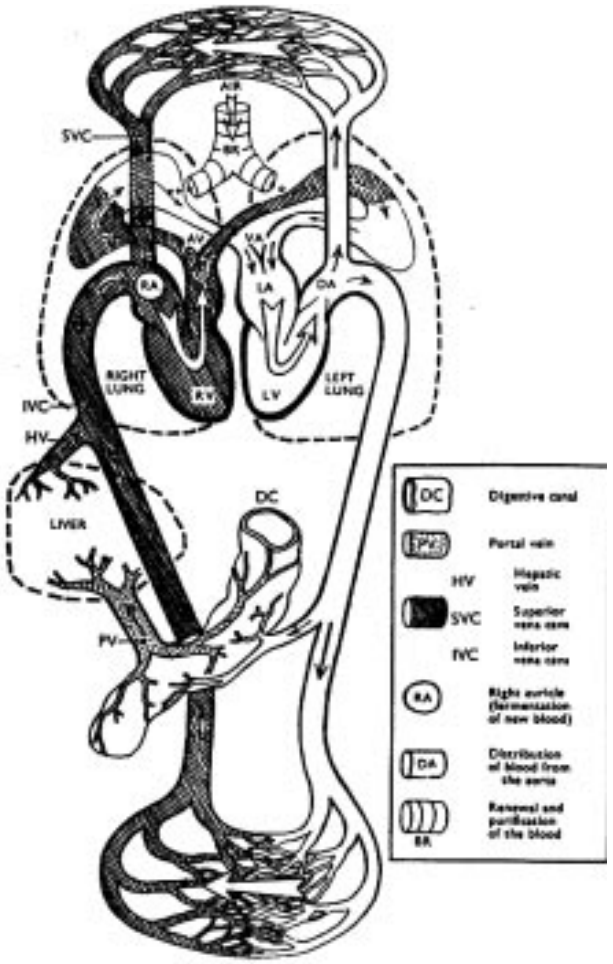

Fig. 1. The circulatory system of the blood as taught by William Harvey in the 17th century. RV, LV: right and left ventricles, respectively. Reproduced with permission, from Chauvois L. William Harvey: his life and times, his discoveries, his methods. New York: Philosophical Library; 1957 (21).

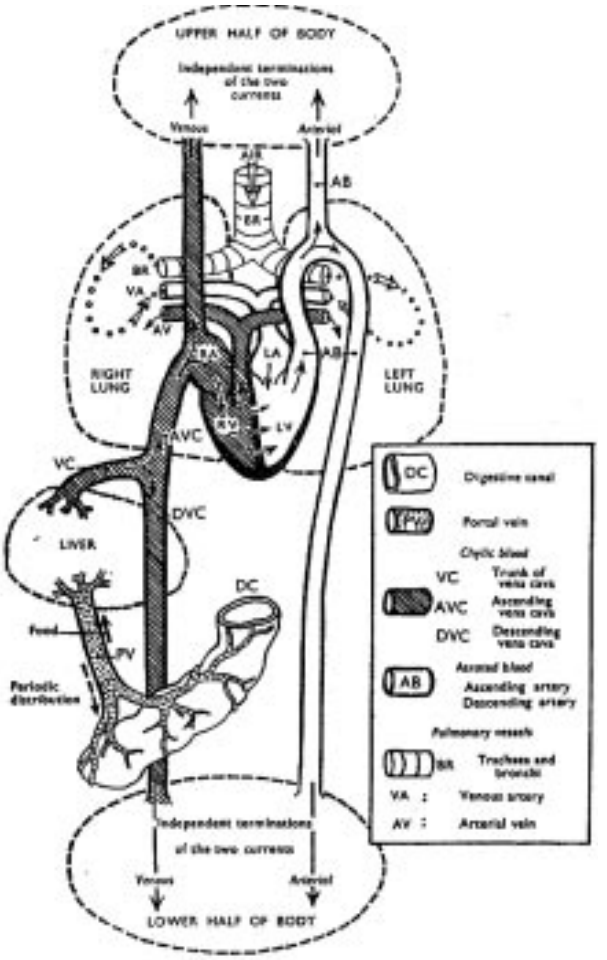

Fig. 2. The traditional system of the movements of blood as taught by Galen in the 2nd century A.D. RA, LA: right and left auricles, respectively. Reproduced with permission, from Chauvois L. William Harvey: his life and times, his discoveries, his methods. New York: Philosophical Library; 1957 (21).

De motu cordis he even admitted the depth of his fears should his doctrine be ill-received (1):

> What remains to be said on the quantity and source of the transferred blood, is, even if carefully reflected upon, so strange and undreamed of, that not only do I fear danger to myself from the malice of a few, but I dread lest I have all men as enemies, so much does habit or doctrine once absorbed, driving deeply its roots, become second nature, and so much does reverence for antiquity influence all men.

Many of Harvey's most accomplished peers challenged his theory. Now that his model has survived for almost 400 years as the key to understanding much of physiology, disease and therapy, one might ask, what influenced his critics? Why did his advocates support him, and why did his adversaries oppose his new idea? In this paper, I will identify common motives that influenced some of Harvey's most prominent critics within the scientific community during his lifetime. Yet this controversy may be worth a closer look for reasons that transcend the immediate issue of Harvey's new theory. For the episode also marks the birth of modern medical science.

Proponents — Experimentation and the Scientific Method

Four centuries ago, scientific investigation hardly resembled that of today. In Europe, mysticism played a legitimate role in scientific rationale (4) and astrology was a required subject at some medical schools. Investigation was unstructured, and eloquent theory sufficed as

proof for new doctrines (5). It was in 1620 that Francis Bacon first described inductive reasoning—the basis of the scientific method that guides research today (3, 6). Of course, scientists had utilized experimentation long before Harvey, Galen among them. Yet its prominence had waned for centuries, and it did not begin to reemerge from its long eclipse until the late 1500s, with the efforts of investigators like Andreas Vesalius and Galileo Galilei (3, 7).

With *De motu cordis*, Harvey set a new standard of investigation by employing experimentation and quantitative reasoning to defend his theory (2, 3, 8). In chapter 9, he used volumetric measurements to calculate the cardiac output. This was the cornerstone of his argument, as he reasoned that in the absence of circulation, the quantity of ingested food alone was not enough to account for the total cardiac output during several minutes or longer; this output far exceeded the blood volume of the body. This rationale, together with the knowledge that valves prevent retrograde bloodflow in veins, enabled Harvey to conclude that blood must circulate (1).

The logic of Harvey's theory impressed many in the medical community (9–11). Yet the most compelling aspect of his argument was his use of experimentation, due to its reproducibility. Using autopsy and vivisection, many of Harvey's colleagues became vocal supporters. Among them were Johannes Walaeus (9), Herman Conring (10), Andrea Argoli (11), Johan Vesling (12), Henry Power (13) and Fortunatus Vopiscus Plemp (10).

Plemp's case illustrates the impact of experimental evidence in this debate. Plemp, a medical professor in Louvain who initially opposed the circulation theory, ironically converted while challenging one of Harvey's adherents, Rene Descartes (10). Descartes, a mathematician and philosopher, read *De motu cordis* and declared his approval in *Discourse on method* (1637), with some modifications (14). In *Discourse*, Descartes rejected Harvey's notion of forceful systole. Instead, he explained that "natural heat implanted by God in the heart" caused blood to vaporize and expand, resulting in diastole. This vaporization then propelled the blood forward, "…causing all the branches of the arterial vein [pulmonary artery] and the grand artery [aorta] to swell almost at the same time as the heart. Immediately after, the heart deflates as do these arteries, because the blood that has entered them has grown cold" (14).

As intricate as Descartes' arguments were, they lacked the support of experimental evidence (12). Furthermore, he incorrectly concluded that blood is ejected at the peak of ventricular diastole.

Descartes sent a copy of his *Discourse* to Plemp. Plemp responded, challenging his claims on the heat of the heart and vaporization of blood. This disagreement enticed Plemp to investigate the matter firsthand, employing vivisection. Plemp's observations disproved Descartes' claims, and he became an adherent of Harvey's doctrine (10).

In the years following publication of *De motu cordis*, medical schools began to accept the practice of anatomical investigation (15). This acceptance of experimentation and anatomical study may well be Harvey's greatest contribution to the scientific method. Interestingly, it was achieved predominantly by Harvey's followers as they attempted to duplicate his findings and conclusions. Their meticulous attempts to replicate his experiments spawned new experiments, and they thereby perpetuated his investigatory style (7, 15).

Proponents — Eccentric Rationale

As exampled by Descartes and Plemp, proponents accepted Harvey's theory for varying reasons. Furthermore, despite the praise afforded to Harvey for his use of experimentation and quantitative methods, many agreed with him for reasons other than those set forth in *De motu cordis*.

Robert Fludd, a friend of Harvey and a fellow London physician, wrote the first published acceptance of the circulation theory (12). Fludd was an active member of the Rosicrucians, a religious movement based on mystical tenets. He turned to the cabalistic principles of polarity and angels to explain the expansion and contraction of the vessels (4). Fludd also relied on astrology and alchemy to explain phenomena, and likened the circulation of blood to the orbits of the cosmos (16). His approval of Harvey's theory, while enthusiastic, has been attributed to the fact that it affirmed his own mystical views on circular motions (12, 16).

Still, Harvey's theory gained popularity through such writings. In 1611, Caspar Bartholin wrote a very successful textbook of anatomy, *Institutiones anatomicae*. Ultimately, his son, Thomas Bartholin, wrote a new edition of the book containing accounts of recent discoveries, including that of circulation. With this

new edition (9), he has been credited with "publish[ing] in 1641…the first textbook containing an exposition of Harvey's doctrine," through which he "introduced Harvey's doctrine into Denmark."

However, it wasn't until a later edition, published in 1651, that Thomas Bartholin actually conceded the existence of circulation. Moreover, his beliefs continued to differ significantly from Harvey's. Bartholin argued that the interventricular septum was permeable, and he was reluctant to classify the heart as a muscle (9). Medical historian Roger French suggests that Bartholin was influenced by an unwillingness to disturb the reputation of his father's text, and by his uncle, Oluff Worm, an adherent of ancient doctrine who opposed the concept of circulation. In fact, according to French (10):

> …Bartholin never fully accepted a Harveian position…. In essence, Bartholin waited until he saw that the circulation controversy was almost settled in Harvey's favor before accepting, because so many others were doing so, that it represented truth. Then it became important for him to weave it into his textbook.

Like Bartholin and Descartes, other proponents accepted Harvey's theory only with modifications. For example, Franciscus Sylvius believed that food, converted and transported to the heart in the form of chyle, was transformed into blood via the "fire" of the right ventricle. As French argues, the reason many of these individuals agreed with some aspects of Harvey's theory and disagreed with other aspects, was that they had different natural philosophies (10).

Opponents

As was the case among proponents, Harvey's opponents also had various reasons for disagreeing with his theory. James Primrose, an indefatigable critic, published a dissent to *De motu cordis* in 1630 containing numerous objections commonly voiced by Harvey's opponents. He argued that the doctrine was a "novelty" and only served to "destroy" traditional medicine. Furthermore, he maintained that circulation would be detrimental in conditions such as fever, by repeatedly and inappropriately delivering "putrid" material to the entire body. Primrose even took aim at the backbone of Harvey's argument, objecting that his calculation of cardiac output was too variable from beat to beat (10). Primrose's aversion to experimentation, however, left him without evidence to support his criticisms (10, 17, 18).

Author Geoffrey Keynes contends that Primrose simply was "congenitally unable to accept new ideas" (12). While this statement reflects the frustration experienced by historians regarding Primrose's obstinacy in rejecting the theory of circulation, it does not address his motives. Primrose was raised in France and ultimately moved to England. When he joined the College of Physicians in London in 1629, Harvey was one of his examiners. At that time, foreigners, regardless of qualification, were prevented from becoming more than licentiates in the College (19). Nonetheless, Primrose soon persuaded the king to permit him to lecture on medicine in public, an appointment the college reacted to with embarrassment (12). They forced him to stop lecturing, explained that he was unqualified because he was merely a licentiate (10), and barred him from candidature in the college. This struggle for acceptance into the college, as well as the presence of Harvey as one of his initial examiners, may be one reason why Primrose adopted such vehement opposition to Harvey's theory (19).

It is interesting to note that, despite Harvey's membership and committed involvement in the college, his theory was not entirely embraced by its members. During the early 17th century, the College of Physicians served the purposes of protecting its members and monopolizing the practice of medicine by fending off competitors, such as surgeons and apothecaries (5, 10, 19). Physicians traditionally were educated differently than their competitors, with much teaching focused on the principles propagated by Hippocrates and Galen. The college learned to exploit this difference, citing such knowledge as a requisite for proper training. Thus, the college became heavily invested in the classical teachings (5). In fact, fines could be imposed upon practitioners who veered from the teachings of this "rational medicine" (10). Pressure to adhere to classical doctrine is evidenced by the fact that some teachers of anatomy failed to address Harvey's theory altogether (10, 12). Moreover, twelve years after *De motu cordis* was published, the president of the college, in front of Harvey, neither approved nor condemned one candidate's thesis because it promoted circulation (12). French goes so far as to suggest that perhaps Harvey

had *De motu cordis* printed overseas for fear of preaching unorthodox views at home (10).

Adherence to ancient doctrine extended beyond England, as evidenced by Caspar Hofmann, a professor of medicine at the University of Altdorf in Germany. During Harvey's trip to continental Europe in 1636, Hofmann agreed to observe a public experiment at which Harvey was to demonstrate proof of circulation. Hofmann promised to reveal his opinion after he had seen the demonstration. The experiment ensued on May 19, but Hofmann remained unconvinced (20).

Historians have had difficulty citing reasons for Hofmann's opposition. On the day of the experiment, Hofmann wrote a short letter to Harvey in which he gave little explanation to justify his disagreement, other than to say ambiguously that circulating blood implied nature's futility in "abound[ing] in unnecessary things" (20). Hofmann disagreed with Harvey because he did not see the purpose of circulation, and believed that such a process would "re-cook" the blood and convert it to bile. Furthermore, by calculating cardiac output, Harvey may have "tried to quantify the unquantifiable," in Hofmann's mind. Hofmann believed that blood became "ebullient" in the heart, and therefore felt it was impossible to accurately measure the volume of blood in or expelled from the heart at any given time. Like others, Hofmann also was troubled by Harvey's lack of evidence of any arteriovenous anastomoses (2, 9, 20). Thus, Hofmann rejected circulation because he opposed Harvey's quantitative evidence, lacked proof of the existence of capillaries, and was committed to a traditional but erroneous conception of cardiovascular physiology.

Opposition to Harvey's new ideas, while persistent, was actually fairly mild, in large measure because he avoided any theological implications in his conclusions. Some 75 years earlier, in 1553, Spanish physician and theologian Michael Servetus had described the pulmonary transit of blood in his publication *Christianismi restitutio* (21). However, his work was basically a theological treatise that challenged traditional religious beliefs; it offended Catholics and Protestants alike (22). Fleeing from the Inquisition in France, Servetus came to Geneva, Switzerland, where John Calvin, the Protestant reformer, having read his book, had him arrested and burnt at the stake. Most copies of the book were soon destroyed (21). Had Servetus been able to separate religion from science, it is possible that his discovery of the pulmonary circulation would have been recognized and appreciated.

As it was, Servetus' discovery remained unknown to Harvey (2). *De motu cordis* did not arouse comparable opposition from the Church of England, perhaps because the work was virtually devoid of religious references. Yet this very lack of religious references appears to have motivated at least one of Harvey's critics. Emilio Parigiano, a respected member of the Venetian College of Physicians, criticized the circulation theory for a number of reasons. As a devout Christian, Parigiano maintained a generally theological interpretation of phenomena. He believed Harvey's naturalistic account of the circulation to be misguided because it failed to incorporate a divine rationale for such a system (10). Moreover, Harvey derived much of his analytical approach from the teachings of Aristotle, a polytheist. To Parigiano, this "promotion" of Aristotelian views may have made Harvey's ideas especially objectionable (8).

Given the conventions of the time, it is understandable that Harvey's experiments were greeted with suspicion. Parigiano, among others, opposed the process altogether. He argued that Harvey had been misled by drawing conclusions from the anatomy of animals. Not only were animals "imperfect" creatures that were "distant" from man, but Harvey's experiments were unnatural, failing to replicate the actual functions of the parts as they existed in nature (10):

> Good God! Is this a valid mode of experience, when the hearts of these creatures have been torn from their bodies, exposed to the air, lacerated, and are lying exhausted and half dead on the table or in the hand, devoid of blood and spirits?

"Territorialism" may also have been a factor in Parigiano's rejection of Harvey's ideas. Although the College in London did not uniformly endorse Harvey's theory, it may have appeared that way to Parigiano. Given his loyalty to the Venetian College of Physicians, he may have been offended by Harvey's address of *De motu cordis* to "Doctor Argent, the excellent and accomplished President of the Royal College of Physicians [in London], and…his esteemed colleagues" (1). Simply put, his rejection of the doctrine may have been partly due to his fear that the authority of the Venetian College of Physicians was threatened by its counterpart in London (10).

Harvey's most ardent opponent was Jean Riolan, a distinguished anatomist from Paris, and a teacher of Primrose. Riolan challenged *De motu cordis* in his *Opuscula anatomica nova* (1649) (23). As a prominent teacher, dean of the Medical Faculty in Paris, the son of a physician, and himself physician to Marie de Medici, Riolan was professionally invested in the ancient doctrines to which he had subscribed and which he had taught throughout his career (10, 17, 24). As a teacher and dean, he was entrusted with propagating these conservative teachings for reasons similar to those of the College of Physicians in London (10).

Ultimately, Riolan proposed his own circulation theory. In deference to antiquity, he still maintained that blood was produced in the liver, the interventricular septum was permeable, and pulmonary circulation did not exist. Although he conceded some movement of blood from arteries to veins in the periphery, he denied any flow of blood through the abdominal organs and argued that only a few drops of blood were expelled from the heart with each beat (17). As with others, Riolan's arguments lacked experimental backing. Like Bartholin, Riolan may have conceded some form of circulation only because of the changing consensus among his peers (10).

In the search for common motives affecting the reception of Harvey's doctrine, it is difficult to miss the striking differences in age between his supporters and opponents. Other authors have referred to this phenomenon as well (9, 11, 12). Both Weil (25) and Keynes (12) have provided valuable lists of Harvey's critics during his lifetime. The vast majority of supporters were 40 years of age or younger in 1628, the year *De motu cordis* was published. Conversely, virtually all the opponents were older than 40 at the time of publication. Notable exceptions include Fludd and Argoli, both supporters, aged approximately 54 and 58 years, respectively, in 1628. Primrose, a critic, was about 30 years old. So it may not have been age per se as much as relative openness to new ideas and methods that distinguished Harvey's supporters from his opponents. New ideas were in the air, in the early 1600s, for those willing to learn.

Summary of Motives

Other than their relative youth, factors common among Harvey's proponents included a willingness to do firsthand experimentation and an openness to quantitative evidence and the scientific method. However, religious and mystical beliefs also played important roles for some proponents, despite Harvey's lack of reference to such beliefs in *De motu cordis*. Lastly, we see that shifting public opinion probably convinced at least some who were otherwise reluctant to accept the new theory.

Harvey's opponents were often heavily invested in ancient doctrine, and may have feared professional repercussions by accepting the circulation theory. Some simply felt there was a lack of clinical application of this new theory. Others disagreed because they saw no evidence of a connection between arteries and veins through which blood could return to the heart. Ironically, some were altogether opposed to experimentation, largely considered today the most convincing component of Harvey's argument. Still other critics were motivated by religion, professional territorialism, and personal resentments.

Conclusion

Among Harvey's critics, there were various motives for agreeing or disagreeing with his ideas. While there were common motives within each group, by no means were all proponents, for example, united in their arguments for the new doctrine. Motives varied, and at times proponents even disagreed with one another. Since its publication, scrutiny of *De motu cordis* has allowed us to confidently accept Harvey's revolutionary doctrine as the basis for the modern understanding of human anatomy and physiology. We have both Harvey and his proponents to thank for this. However, we must also thank his critics, for as a result of their challenges, members of the scientific community began to embrace experimentation and accept the scientific method, to evaluate his doctrine. These serve as the two pillars of today's attempts to understand the biological basis of medicine. Few controversies have proved more fertile or influential in shaping the future.

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